PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PF-0712 PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/16644	15 June 2000 (15.06.2000)	17 June 1999 (17.06.1999)
International Patent Classification (IPC) or national classification and IPC		
IPC(7): C07K 14/00; C07H 17/00; C12P 21/06 and US Cl.: 530/350;, 387.1; 536/23.1; 435/ 69.1		
Applicant		
INCYTE GENOMICS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09 January 2001 (09.01.2001)	09 September 2003 (09.09.2003)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Karen Cochrane Carlson, Ph.D. Telephone No. 703-308-1235

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/16644.

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description:
pages 1-75 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 76-78, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages 79/1-79/8, filed with the letter of 05 October 2001 (05.10.2001)

☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-23, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-27 drawn to sequences other than SEQ ID NO: 1 and Claims 28-90

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-27 other than the subject matter of SEQ ID NO: 1 and Claims 28-90

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-27	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-27	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-27	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-27 drawn to SEQ ID NO: 1 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest SEQ ID NO: 1 as determined by the European Search Authority.

---------- NEW CITATIONS ----------

a) exposing a sample comprising a polypeptide of claim 1 to a compound, and

b) detecting antagonist activity in the sample.

23. A pharmaceutical composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

24. A method for treating a disease or condition associated with overexpression of functional RMEP, comprising administering to a patient in need of such treatment a pharmaceutical composition of claim 23.

25. A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:

a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.

26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:

a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,

b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.

27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, and

b) detecting altered expression of the target polynucleotide.

28. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

29. A method for assessing toxicity of a test compound, said method comprising:

a) treating a biological sample containing nucleic acids with the test compound;

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

c) quantifying the amount of hybridization complex; and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

30. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:1.

31. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:2.

32. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:3.

33. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:4.

34. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:6.

35. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:7.

36. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:8.

37. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:9.

38. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:10.

39. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:11.

40. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:12.

41. A method of claim 9, wherein the polypeptide has the sequence of SEQ ID NO:13.

42. A diagnostic test for a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a biological sample comprising the steps of:

a) combining the biological sample with an antibody of claim 10, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

43. The antibody of claim 10, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a $F(ab')_2$ fragment, or

e) a humanized antibody.

44. A composition comprising an antibody of claim 10 and an acceptable excipient.

45. A method of diagnosing a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a subject, comprising administering to said subject an effective amount of the composition of claim 44.

46. A composition of claim 44, wherein the antibody is labeled.

47. A method of diagnosing a condition or disease associated with the expression of human RNA metabolism proteins (RMEP) in a subject, comprising administering to said subject an effective amount of the composition of claim 46.

48. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibodies from said animal; and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

49. An antibody produced by a method of claim 48.

50. A composition comprising the antibody of claim 49 and a suitable carrier.

51. A method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 or an immunogenic fragment thereof, under conditions to elicit an antibody response;

b) isolating antibody producing cells from the animal;

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;

d) culturing the hybridoma cells; and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

52. A monoclonal antibody produced by a method of claim 51.

53. A composition comprising the antibody of claim 52 and a suitable carrier.

54. The antibody of claim 10, wherein the antibody is produced by screening a Fab expression library.

55. The antibody of claim 10, wherein the antibody is produced by screening a recombinant immunoglobulin library.

56. A method for detecting a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 in a sample, comprising the steps of:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 in the sample.

57. A method of purifying a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 from a sample, the method comprising:

a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and

b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13.

58. A microarray wherein at least one element of the microarray is a polynucleotide of claim 12.

59. A method for generating a transcript image of a sample which contains polynucleotides, the method comprising the steps of:

a) labeling the polynucleotides of the sample,

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b) contacting the elements of the microarray of claim 58 with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex, and

c) quantifying the expression of the polynucleotides in the sample.

60. An array comprising different nucleotide molecules affixed in distinct physical locations on a solid substrate, wherein at least one of said nucleotide molecules comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of a target polynucleotide, said target polynucleotide having a sequence of claim 11.

61. An array of claim 60, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 contiguous nucleotides of said target polynucleotide.

62. An array of claim 60, wherein said first oligonucleotide or polynucleotide sequence is completely complementary to at least 60 contiguous nucleotides of said target polynucleotide.

63. An array of claim 60, which is a microarray.

64. An array of claim 60, further comprising said target polynucleotide hybridized to said first oligonucleotide or polynucleotide.

65. An array of claim 60, wherein a linker joins at least one of said nucleotide molecules to said solid substrate.

66. An array of claim 60, wherein each distinct physical location on the substrate contains multiple nucleotide molecules having the same sequence, and each distinct physical location on the substrate contains nucleotide molecules having a sequence which differs from the sequence of nucleotide molecules at another physical location on the substrate.

67. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.

68. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:2.

69. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:3.

70. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:4.

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71. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:6.

72. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:7.

73. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:8.

74. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:9.

75. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:10.

76. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:11.

77. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:12.

78. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:13.

79. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:14.

80. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:15.

81. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:16.

82. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:17.

83. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:19.

84. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:20.

85. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:21.

86. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:22.

87. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:23.

88. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:24.

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89. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:25.

90. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:26.